DONOR
NETWORK OF ARIZONA

The vital link for organ, tissue and eye recovery

January 18, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rm. 1061
Rockville, MD 20852

Re: Suitability Determination for Donors of Human Cellular and Tissue-Based Products
Docket Number 97N-484S

Dear Sir or Madam:

Donor Network of Arizona is thankful for the opportunity to provide written commentary concerning the pending regulatory action found in docket 97N-484S. As a leader within the transplant community, Donor Network of Arizona hopes to offer insightful and beneficial commentary regarding this docket. This pending action addresses a specific need for enhanced medical and social screening for donors of human cellular and tissue-based products.

I. Historical Background

Donor Network of Arizona was founded as a transplant organization dedicated to the most stringent and most advanced levels of excellence in organ, eye and tissue transplantation. Donor Network of Arizona is federally designated as the Organ Procurement Organization for the state of Arizona, is accredited with the Eye Bank Association of America and follows the guidelines set forth by the American Association of Tissue Banks.

Since 1994, Donor Network of Arizona is responsible for greater than 8,000 corneal tissues recovered and processed for transplant, recovery of greater than 1,000 tissue donors for transplant and a transplant recovery program resulting in the transplantation of 1,480 organs. Throughout its existence, Donor Network of Arizona has supported the Food and Drug Administration's oversight of human tissue-based products and feels that such regulation only further enhances the safety of human tissue recovered, processed and transplanted in our medical community.

3877 N. 7th Street #200 • Phoenix, Arizona 85014 • 602.222.2200 • Fax 602.222.2202 • 1.800.94.DONOR
www.dnaz.org

II. Comments Directed to Proposed Rules

A. **General Requirements - Donor Medical History Interview and Legislative Consent, (Section 1271.3(o) and 1271.75(d))**

The FDA should require that a donor medical history interview be performed on **all** donors of tissue-based products. There should be no exception to this interview for donor tissue procured under legislative consent. Autopsy and medical record review alone is insufficient and inconsistent in its ability to accurately identify signs and symptoms of transmissible diseases such as rabies, tissue spongiform encephalopathy (TSE), human immunodeficiency virus (HIV) and viral hepatitis. Donor Network of Arizona has never procured donor tissue under legislative consent and has never found that our ability to meet the surgical demands of our transplant community to be compromised. If there is to be any loss of donor tissue associated with the performance of a donor medical interview on all donors, including those falling under the jurisdiction of legislative consent, it is far outweighed by the value the donor medical history interview holds for medical and social screening.

The donor medical history interview is a vital screening tool, whose contribution to a tissue-based screening process is imperative. Donor Network of Arizona has conducted such an interview for each eye, tissue and organ donor for transplant since 1994. During this span, thousands or organ and tissue donors have been screened for transplant purposes.

The donor medical history interview is valuable as it offers another method by which behavior suspicious of infectious disease may be identified. Such medical history interview questions indicative of TSE or Rabies include:

1. Did the deceased have any of the following symptoms: Change in cognition (i.e. change in perception, reasoning or judgement, etc.), cerebellar dysfunction (i.e. impairment of muscular movements, wide-based gait, etc.), speech abnormalities; or upper motor neuron signs such as myoclonus (i.e. muscle twitching, tremors, etc.)?

2. Has the deceased or any of the deceased's blood relatives been diagnosed with or told they were at increased risk for Creutzfeldt-Jakob Disease (CJD)?

3. Did the deceased ever receive a human or animal organ or tissue transplant, e.g. kidney, heart, liver, bone, cornea, **human dura mater**, skin, etc.?

4. Did the deceased ever receive human pituitary-derived growth hormone?

5. Was the deceased ever bitten by an animal which could have carried the rabies virus (dogs, mice, rats, bats, etc.)?

Such medical history or behavioral questions indicative of HIV or viral hepatitis include, but are limited to:

1. In the past 12 months, has the deceased lived with anyone who had been told they had hepatitis?

2. In the past 12 months, did the deceased have sex even once, or close contact with any persons known or suspected to have hepatitis or HIV infection?

3. In the past 5 years, did the deceased have sex, even once with another male?

In deference to space and time constraints, Donor Network of Arizona will cite but one example, of the hundreds, whereby donor tissue has been ruled unsafe for transplant based solely upon the medical history interview. A potential donor for multiple tissues had been referred to our facility from a local hospital. The patient's primary cause of death was unambiguous, the death certificate was to be signed by the attending physician and an autopsy was not required, nor requested. The donor's medical records had been reviewed without any signs of concern. A routine medical history interview was conducted with the potential donor's living next-of-kin. Within the context of this dialogue, the next-of -kin indicated that the potential donor did have a blood relative (sister) who had been diagnosed with and who had died from Creutzfeldt-Jakob Disease. The potential donor tissue was immediately identified as unsuitable and unsafe for transplantation. This information would not have been elucidated from any other common medical history source, such as the donor medical record, physical assessment, or if performed, the autopsy. This example highlights and emphasizes the need for a medical history interview on all potential donors of human tissue products.

If a portion our ethical and medical responsibility is to protect the public community that we serve from the transmission of potentially lethal viral and prion diseases, how could we ever bypass the opportunity to investigate such medical history and social behavior? Realistically, could medical records and pathological information alone consistently and accurately reveal answers to any of the above screening questions? Granted, the incidence of a certain number of these diseases is minimal within the United States, however, that does not absolve or alleviate our professional and ethical duty to protect the community that we serve from lethal disease transmission. If increased regulations for medical history interviews mean the prevention of only one disease transmission in thousands, then that is one life saved and well worth the effort.

B. General Requirements - Donor Specimen Collection at time of recovery or within 48 hours of recovery (Section 1271.80(b))

Donor Network of Arizona would like to express grave concern regarding blood specimen collection at the time of or within 48 hours of tissue recovery. Often, potential donors are hospitalized prior to expiration, whereby the donor is closely monitored and exposure to relevant communicable disease is limited. Moreover, all hospital medical records are intensely scrutinized and any evidence of exposure to communicable disease is acted upon appropriately by the Eye or Tissue Bank representative.

Post-mortem (cadaveric) blood samples often suffer from mild to severe red blood cell hemolysis. Such hemolysis invariably interferes with serological testing for infectious diseases, especially Hepatitis B Surface Antigen and HIV-1 p24 Antigen. Use of post-mortem specimens for serological testing only increases the likelihood of inaccurate testing results. Further, some post-mortem samples may not pass defined algorithms for plasma dilution, in which case a pre-mortem or pre-infusion sample would be required. For these reasons, the FDA should allow the use of pre-mortem or pre-infusion specimen collection.

C. Donor Testing - TSE testing for Corneal Tissue

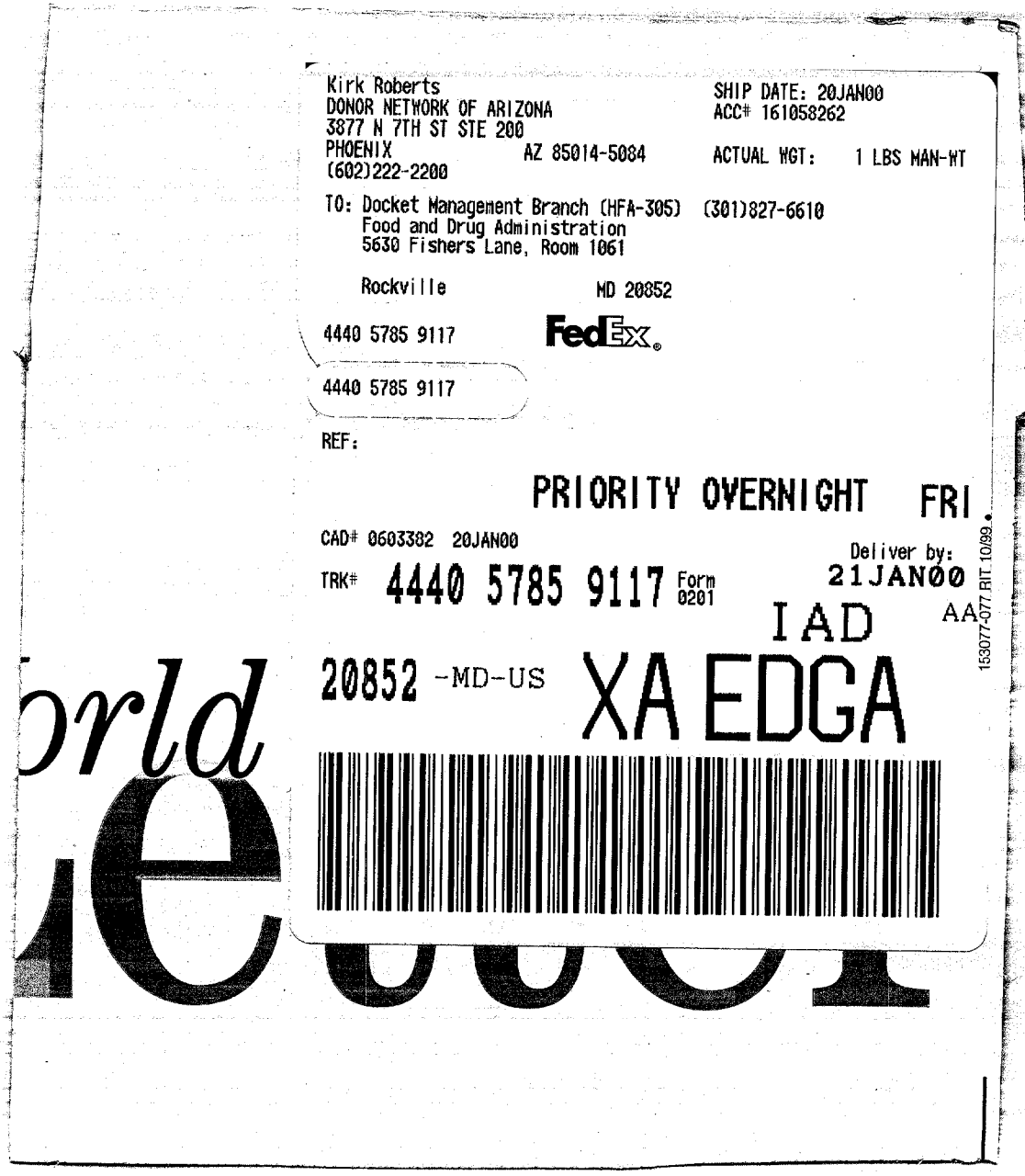
Currently, TSE testing is not a feasible option for corneal tissue donors. The duration of time for complete and accurate full brain autopsy is not compatible with corneal tissue storage life. Rather, use of **all** available screening components including the medical screening interview would satisfactorily substitute for TSE screening in lieu of a full brain autopsy on corneal tissue donors.

III. Summary

Donor Network of Arizona applauds the goals and the intentions set forth by the FDA regarding its regulatory oversight of human tissue-based products. What is of vital importance is to enforce final action upon such proposed regulations based upon the need to prevent the transmission of lethal infectious disease via human tissue transplantation. Working collectively with the FDA, Eye and Tissue Banks with their respective associations can ensure the safety of recovery, processing and transplantation of human tissue-based products.

Sincerely,

Kirk A. Roberts, BS, CEBT
Quality Systems Manager
Donor Network of Arizona



Kirk Roberts
DONOR NETWORK OF ARIZONA
3877 N 7TH ST STE 200
PHOENIX AZ 85014-5084
(602)222-2200

SHIP DATE: 20JAN00
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ACTUAL WGT: 1 LBS MAN-WT

TO: Docket Management Branch (HFA-305) (301)827-6610
Food and Drug Administration
5630 Fishers Lane, Room 1061

Rockville MD 20852

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